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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	20

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/537,654	MAHAJAN ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-10,12,14 and 16-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-10,12,14 and 16-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment to the claims requested in Paper No. 19, filed 9 May 2003 have been entered. That amendment indicates that claim 11 is withdrawn; however claim 11 was cancelled in the amendment filed 15 April 2002. Claims 2-10, 12, 14 and 16-34 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment and Arguments

3. The rejection of claims 2-10, 12, 14 and 16-34 under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is WITHDRAWN in light of Applicant's pointing to support for the phrases "over the entire length of SEQ ID NO:1" and "full-length complement of SEQ ID NO:1" and amendment to replace "participates in a complex which enhances recombinase activity".

Claim Rejections - 35 USC § 112

4. Claims 2-10, 12, 14, 16, 18-26 and 28-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO:1 or that encode SEQ ID NO:2, does not reasonably provide enablement for nucleic acids that have 90% identity to SEQ ID NO:1, that encode a protein that has 90% identity to SEQ ID NO:2, or that hybridize to SEQ ID NO:1. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 5 February 2003, as applied to claims 2-10, 12, 14-16, 18-26 and 28-35. Applicant's arguments filed 9 May 2003 have been fully considered but they are not persuasive.

Applicant urges that the specification provides enablement for nucleic acids that have 90% identity to SEQ ID NO:1, that encode a protein that has 90% identity to SEQ ID NO:2, or that hybridize to SEQ ID NO:1 and guidance is found in SEQ ID NOs:1-6, and the specification on pg 1-4, 6-9, 11, 14-15, 17-22, 24, 26, 28-29, 33-37, 58 and 60. Applicant also submitted Appendices C and D in the response filed 15 April 2002, and submit Appendix E showing a global alignment of the instant proteins with other RAd51C proteins (response pg 8-9).

This is not found persuasive because the specification on pg 1-4, 6-9, 11, 14-15, 17-22, 24, 26, 28-29, 33-37, 58 and 60 only provides general guidance, not guidance specific to the instant nucleic acid. SEQ ID NOs:3 and 5 are 98.9% and 98.6% identical, respectively, to SEQ ID NO:1, and thus do not provide guidance for making nucleic acids with 90% identity to SEQ ID NO:1. The DNA repair proteins shown in the alignments of Appendices D and E have so little sequence similarity to SEQ ID NO:2 that they also provide no guidance for making nucleic acids with 90% identity to SEQ ID NO:1.

Applicant urges that like Hill and Lazar one would use these alignments to identify conserved, partially conserved and non-conserved amino acids to predict which substitutions would affect the function of the protein. Applicant points out that Lazar and Hill both use known

homology to identify and target particular amino acids, showing that one of skill in the art believes that structural identity is predictive of protein function (response pg 9-10).

This is not found persuasive. Hill et al made substitutions in three histidines that are maintained in ADP-glucose pyrophosphorylase across several species; one would expect that such an amino acid could tolerate no or only conservative substitutions. However, substitution with the "nonconservative" amino acid glutamine resulted in little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). Thus, Hill et al teach that reliance on sequence homology for making amino acid substitutions is unpredictable.

Applicant urges that undue experimentation is not necessary to practice the invention; the sequences have been defined by physical and chemical properties, that is sequence identity to SEQ ID NO:1 and functional activity. This can be used with common techniques to practice the full breadth of the invention. Applicant also urges that some experimentation is permitted (response pg 10-11).

This is not found persuasive because the specification does not teach any nucleic acids that have 90% identity to SEQ ID NO:1, that encodes a protein that has 90% identity to SEQ ID NO:2, or that hybridize to SEQ ID NO:1.

Furthermore, RAD51 proteins are thought to have similar cellular functions to RecA (instant specification, pg 3, lines 3-16, and Thacker et al, 1999, Trends in Gen. 15:166-168). Plants transformed with a gene encoding the RecA protein unexpectedly do not have increased gene targeting, even though the plants had increased levels of intrachromosomal recombination (Reiss et al, 2000, Proc. Natl. Acad. Sci. 97:3358-3363, pg 3360-3362).

5. Claims 2-10, 12, 14, 16, 18-26 and 28-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 5 February 2003, as applied to claims 2-10, 12, 14-16, 18-26 and 28-35. Applicant's arguments filed 9 May 2003 have been fully considered but they are not persuasive.

Applicant urges that the claims now recite functional language wherein the nucleic acid encode a protein involved in DNA double strand break repair; thus, the claims follow the format of Example 14 of the Guidelines. Applicant also asks why 95% sequence identity is an acceptable structural parameter, while 90% is not and why enzyme catalysis is an acceptable function while involvement in a non-enzymatic component of a complex is not an acceptable functional parameter. Applicant urges that recitation of at least 90% sequence identity is a predictable and easily quantifiable structure (response pg 12-13).

This is not found persuasive. What is the nature of the "involvement"? Proteins that "are involved" in DNA repair might recognize different kinds of DNA damage, might activate DNA repair proteins, might do any of the enzymatic steps required to physically repair the DNA. Which does the instant protein do? The specification does not describe any nucleic acids that have 90 or 95% identity to SEQ ID NO:1, that encode a protein that has 90 or 95% identity to SEQ ID NO:2, or that hybridize to SEQ ID NO:1 under the recited conditions.

Applicant urges that recitation of explicit high stringency hybridization and wash conditions follows the guidelines of claiming sequences by a structural parameter, and Applicant has disclosed two other sequences that would hybridize to SEQ ID NO:1 (response pg 13).

This is not found persuasive because SEQ ID NOs:3 and 5 are 98.9% and 98.6% identical, respectively, to SEQ ID NO:1, and thus do not describe nucleic acids with 90% identity to SEQ ID NO:1, wherein the nucleic acids encoding proteins with the claimed function. Furthermore, the hybridization conditions lack hybridization and wash times, making it very unclear what nucleic acids are being claimed.

Applicant urges that not every species encompassed by the claims need be disclosed; and description of a representative number does not require individual support for each species. Applicant urges that their language is sufficient to satisfy the written description requirement (response pg 13-14).

This is not found persuasive. While it is true that not every species need be described, a representative number within the full range of the claims do need to be described. The specification does not describe the sequence of even a single nucleic acid that has 90% identity to SEQ ID NO:1 or that encodes a protein that has 90% identity to SEQ ID NO:2.

Applicant urges that they have disclosed three nucleic acids encoding Rad51C proteins and have provided guidance for making variants; thus, they urges that they had possession of sequences with 90 or 95% identity to SEQ ID NO: 1 or 2 (response pg 14).

This is not found persuasive because SEQ ID NOs:3 and 5 are 98.9% and 98.6% identical, respectively, to SEQ ID NO:1, and thus do not describe nucleic acids with 90 or 95% identity to SEQ ID NO:1

6. Claims 2-10, 12, 14 and 16-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 5 February 2003, as applied to claims 2-10, 12 and 14-35. Applicant's arguments filed 9 May 2003 have been fully considered but they are not persuasive.

Applicant urges that Ausubel et al, cited in Appendix F, makes clear that one of skill in the art would know what selectively hybridizes refers to and that definiteness must be analyzed in view of the context of the application, the teachings of the prior art and claim interpretation made by one of skill in the art (response pg16).

This is not found persuasive. Ausubel states "time can have an important influence on the result" (pg 2.10.11, right column, paragraph 2). Thus, "high stringency" as recited in the amended claims, is indefinite without recitation of hybridization and wash conditions.

The following rejections are new, as a result of amendments to the claims:

Claims 12, 14 and 25 are indefinite in their recitation of "polypeptide involved in DNA double strand break repair". The nature of that involvement is unclear. Proteins that "are involved" in DNA repair might recognize different kinds of DNA damage, might activate DNA repair proteins, might do any of the enzymatic steps required to physically repair the DNA. Which does the instant protein do?

Claim Rejections - 35 USC § 102

7. Claim 14 remains rejected under 35 U.S.C. 102(a) as being anticipated by NCI-CGAP (1998, GenBank Accession No. AI184177). The rejection is repeated for the reasons of record as set forth in the Office action mailed 5 February 2003. Applicant's arguments filed 9 May 2003 have been fully considered but they are not persuasive.

Applicant urges that the nucleic acid taught by NCI-CGAP would not hybridize to SEQVID NO:1 under the high or low stringency conditions as shown by the global alignment in Appendix G (response pg 17-18).

This is not found persuasive. Given the lack of hybridization and wash times in the claims, almost any DNA sequence would hybridize if the times were appropriately manipulated.

8. Claims 2-10, 12 and 16-34 are free of the prior art given the failure of the prior art to teach or suggest an isolated RAD51C encoding nucleic acid with 90% identity to SEQ ID NO:1 or encoding a protein with 90% identity to SEQ ID NO:2. The prior art also fails to teach or suggest a recombinant expression cassette comprising a nucleic acid that hybridizes to SEQ ID NO:1.

Allowable Subject Matter

9. Claims 17 and 25 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0196.

Anne R. Kubelik, Ph.D.
July 10, 2003

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